Table 1. Total Bile Acid and DLIS Concentrations in 10 Patients with Liver Disease

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age, yr</th>
<th>Total bilirubin, mg/L</th>
<th>DLIS, μg digoxin equiv. per liter</th>
<th>Bile acids, mol/L</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>60</td>
<td>200</td>
<td>0.25</td>
<td>80.5</td>
<td>Carcinoma of the pancreas with hepatic obstruction.</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>75</td>
<td>164</td>
<td>0.16</td>
<td>21.8</td>
<td>Carcinoma of the gallbladder with biliary obstruction.</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>52</td>
<td>154</td>
<td>1.15</td>
<td>110</td>
<td>Cirrhosis with progressive liver and renal failure.</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>43</td>
<td>100</td>
<td>0.41</td>
<td>124.5</td>
<td>Chronic pancreatitis and cholelithiasis. Cirrhosis secondary to alcohol abuse.</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>33</td>
<td>52</td>
<td>0.29</td>
<td>40.6</td>
<td>Liver failure due to biliary cirrhosis. Cirrhosis secondary to alcohol abuse.</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>19</td>
<td>208</td>
<td>0</td>
<td>18.0</td>
<td>Liver failure due to biliary cirrhosis. Cirrhosis secondary to alcohol abuse. Cirrhosis secondary to alcohol abuse with hepatorenal syndrome. Hepatoma.</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>48</td>
<td>316</td>
<td>0.48</td>
<td>116.0</td>
<td>Hepatoma.</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>58</td>
<td>85</td>
<td>1.80</td>
<td>4.7</td>
<td>Cirrhosis secondary to alcohol abuse with hepatorenal syndrome. Hepatoma.</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>20</td>
<td>61</td>
<td>2.50</td>
<td>75.1</td>
<td>Leukemia, renal and liver failure due to disseminated candidiasis and tumor lysis syndrome.</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>36</td>
<td>169</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Significantly higher than normal (≤0.2 μg/L and <10 μmol/L, respectively) in this group of patients. The correlation between DLIS and bile acid concentrations is unimpressive (r² = 0.047) if all patients' results are included. However, if we eliminate the data from the three patients with combined liver and renal impairment, this correlation improves significantly (r² = 0.906). These data suggest that some common pathological mechanism may be responsible for the accumulation of DLIS and bile acids in patients with liver disease. The correlation between DLIS and bilirubin in this group of seven patients was not as high (r² = 0.525).

We have previously determined the cross-reactivity of individual bile acids with the digoxin RIA procedure, using antiseraum DB-157 (3, 6), and we estimate on the basis of our data that bile acids can account for approximately 15% of the DLIS in patients with liver disease. Other as-yet-unidentified cross-reacting steroids probably account for the rest of the DLIS in these patients. In the three patients we investigated who also had renal impairment, the DLIS concentrations were much higher than in the patients who only had impaired liver function: 1.91 ± 0.68 and 0.44 ± 0.36 μg digoxin equivalents per liter, respectively. Renal impairment leads to increased DLIS independent of liver disease (10). Bile acids are an insignificant contributor to DLIS in this situation. Further studies are required to elucidate the biochemical nature of the other DLIS species in liver disease.

References

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Sources of Error in Sodium Measurements
To the Editor:
Following our paper on analytical error in hyponatremia, in which we used two commercial direct ion-selective electrode analyzers (1), Mann and Green (2) reported observing similar discrepancies when using serum samples. They commented however, that...
our use of heparinized plasma may have contributed to the lower sodium results we obtained. According to their discussion, the effect occurs when small samples of blood, e.g., 1 mL, are placed in 10-mL commercial heparinized blood tubes.

The samples used in our study (1) were not pediatric samples and had been analyzed with a Technicon SMAC, an IL 502, a Corning 902, an in-house direct ion-selective electrode system, and an IL 543 flame photometer. The total amount of plasma required for all these analyses was about 1.1 mL—a volume that would have required between 2.5 and 3.0 mL of blood unless particular attention was paid to plasma separation for the samples used in our study. This was not the case, however; all samples had been submitted for routine analysis.

Furthermore, the use of small volumes of blood would have led to a significant positive bias in the results obtained with the in-house system. This system uses the neutral carrier ionophore ETH 227 for sodium, which is highly selective for lithium ions (3). The use of lithium-heparinized blood-collection tubes had been previously studied by assaying aqueous standard solutions, whole blood, and plasma. Various volumes of a 140 mmol/L sodium standard and whole blood were placed in these collection tubes and then analyzed with the in-house system; the plasma was then removed from the whole blood and also analyzed. The flame-photometric value for Na in the plasma sample was 141 mmol/L. The ion-selective electrode results were as follows:

<table>
<thead>
<tr>
<th>Vol of std. or blood added to tube, mL of sample</th>
<th>Aqueous standard</th>
<th>Whole blood</th>
<th>Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 to 3</td>
<td>±1</td>
<td>±1</td>
<td>±1</td>
</tr>
<tr>
<td>2</td>
<td>+2</td>
<td>+3</td>
<td>+2</td>
</tr>
<tr>
<td>1</td>
<td>+6</td>
<td>+8</td>
<td>+9</td>
</tr>
</tbody>
</table>

Clearly, a considerable constant positive bias would have been observed with the in-house system if small sample volumes had been used, irrespective of any heparin binding of sodium. However, this constant bias was not observed (1). Further, the correlation coefficient of 0.93 obtained by Mann and Green shows considerably more random error than our data ($r = 0.98$).

This confirms our belief that our data were not affected by heparin binding of sodium and that the requirement of an international agreement on the standardization of direct ion-selective electrodes is still quite important to their future use.

References


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